UIJ UroToday International Journal®

www.urotodayinternationaljournal.com
Volume 1 - December 2008

Pathogenesis and Diagnosis of Nocturia: From a New Viewpoint

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Submitted on 4 November 2008 - Accepted for Publication on 6 November 2008

ABSTRACT

Nocturia, which affects general health and quality of life, is a symptom often observed not only in patients with benign prostatic hyperplasia, but in the elderly of both genders as well. There are 5 causes of nocturia: (1) nocturnal polyuria, (2) reduction of nocturnal bladder capacity, (3) a combination of 1 and 2, (4) global polyuria, and (5) sleep disorders. To understand the pathogenesis of nocturia, it is important to investigate different factors for each cause. For nocturnal polyuria (1), it is important to investigate excessive fluid intake, hypertension, circadian rhythm of arginine vasopressin (AVP), and cardiovascular conditions based on brain natriuretic peptide (BNP) levels in plasma. For reduction of nocturnal bladder capacity (2), blood pressure and plasma concentrations of melatonin and glycine must be measured. Complicating systemic diseases, such as diabetes mellitus, diabetes insipidus, and polydipsia can, lead to global polyuria (4), and sleep disorders (5) are defined by the quality of sleep, including conditions of arousal and hypnagogic disorders. The purpose of this article is to review the pathogenesis and diagnosis of nocturia, particularly by focusing on other causes than urological fields, which might lead to a better understanding of nocturia. To diagnose and make a therapeutic plan for nocturia, a modified bladder diary, International Prostate Symptom Score (IPSS), King's Health Questionnaire (KHQ), Pittsburgh Sleep Quality Index (PSQI), and a sleeping diary are useful and should be combined with an interview and urological examination.

KEYWORDS: Nocturia, Pathogenesis, Diagnosis

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REVIEW

I. DEFINITION AND EPIDEMIOLOGY OF NOCTURIA

I-1) PATHOLOGICAL CONDITIONS OF NOCTURIA

Nocturia was previously considered a storage symptom associated with benign prostatic hyperplasia (BPH). However, many urologists realize some patients have persistent nocturia after BPH treatment and improvement in bladder outlet obstruction. This suggests that nocturia is a complicated pathological condition caused by multiple factors, and identification of these factors leads to accurate diagnosis and treatment.

I-2) DEFINITION OF NOCTURIA

The International Continence Society defines nocturia as "the complaint that the individual has to wake at night one or more times to void" [1]. In other words, these patients complain of waking at night one or more times to void and are willing to receive treatment. An epidemiological survey conducted in countries other than Japan reported that the percentage of

doi:10.3834/uij.1939-4810.2008.11.07

ISSN 1944-5792 (print), ISSN1944-5784 (online)

persons voiding 3 or more times per night was about 0% in adolescents (13 to 19 years of age), but it increased with age to 11% in people in their 60s and 70s. This percentage appears to be similar in Japan [2,3].

I-3) GENDER DIFFERENCE IN NOCTURIA

Nocturia is a symptom that may occur in both men and women, and it affects men with or without BPH or bladder outlet obstruction. Patients with nocturia may have symptoms of overactive bladder, underactive bladder, or both. There is little or no difference between genders in symptoms; however, women have a smaller functional bladder capacity (maximum voided volume) and thus require a greater number of micturitions to void a certain volume of urine. Accordingly, women are more likely to have storage symptoms, whereas men are more likely to have voiding symptoms [4].

I-4) COMPLICATIONS AND RISKS ASSOCIATED WITH NOCTURIA

A large epidemiological survey conducted in Sweden involving 6143 subjects with a follow-up period of 5.5 years showed that elderly people with 3 or more episodes of nocturia had a mortality twice that of control subjects regardless of gender after adjustment for factors of age, gender, heart disease, diabetes mellitus, and stroke [5]. Another survey reported that arrhythmia, diabetes mellitus, and sequelae of stroke in elderly people were significantly associated with nocturia characterized by 3 or more micturitions at night regardless of gender [6]. A study in women 40 to 64 years of age showed that nocturia was associated with significant increases in the number of visits to physicians, hypnotic use, and sick-leave days and that health condition, feeling of happiness, and future prospects worsened with increasing numbers of voids [7]. Another report indicated that patients with nocturia who voided 2 or more times at night had a decreased physical and mental quality of life, decreased activity, and significantly lower productivity [8]. Elderly people have a significant risk of fracture due to falls at night. Nocturia was reported to increase the risk of falls in patients with cardiovascular disorder, gait disturbance, balance disorder, neurological disorder, muscle and joint disorders, sensory dysfunction, movement disorder, osteoporosis, and mental retardation [9-11]. It was also reported that the risk of nocturnal falls was twice as high in elderly patients with nocturia who voided 2 or more times at night as in persons who voided once or less [12]. With all the findings taken into consideration, the management of nocturia is very important.

II. VOIDING RHYTHM AND VOIDED VOLUME

To elucidate the pathological conditions of nocturia, it is essential to understand normal voiding rhythm and age-related changes. The voiding rhythm has not been established in neonates. The voiding pattern characterized by increased voided volume during the day and decreased voided volume at night is formed during the first few years of life. The volume of urine formed during the day progressively increases, while nocturnal urine formation decreases. Eventually, the number of nocturnal micturitions decreases to zero when the volume of urine formed at night is less than the bladder capacity. At this stage, the diurnal rhythm of arginine vasopressin (AVP) secretion has already been established [13].

The 24-hour urine volume in adults is about 1600 ± 300 mL regardless of gender and does not change greatly with increasing age. The pattern of diurnal variation of voided volume changes substantially with increasing age. The diurnal urine volume (8:00 to 20:00) is about twice as much as the nocturnal urine volume (20:00 to 8:00) in persons in their 30s, but the volumes are similar in persons 65 years of age or older, and the pattern is reversed in some individuals [14]. It should be noted, however, that the voided volume per micturition and number of micturitions vary greatly from person to person regardless of gender.

III. PATHOGENESIS OF NOCTURIA IN ELDERLY PEOPLE

There are 5 categories of nocturia in elderly people: (1) nocturnal polyuria, (2) reduced nocturnal bladder capacity, (3) a combination of 1 and 2, (4) global polyuria, and (5) sleep disorders.

III-1) NOCTURNAL POLYURIA

III-1)-A. Definition of nocturnal polyuria

Nocturnal polyuria may be defined as a nocturnal urine volume that is at least 20% of the total daily urine volume in young people or at least 33% in elderly people, or defined as 6.4 mL/kg or more urine produced during sleep; however, no established definition is available. Underlying diseases include congestive heart failure, diabetes mellitus, sleep apnea, leg edema, excessive fluid intake, nephrosis, hepatic failure, hypoalbuminemia, circadian rhythm abnormalities of catecholamines, and AVP secretion abnormalities.

http://www.urotodayinternationaljournal.com
doi:10.3834/uij.1939-4810.2008.11.07
ISSN 1944-5792 (print), ISSN1944-5784 (online)

III-1)-B. Excessive fluid intake

Excessive fluid intake, which induces an increase in the extracellular fluid volume and subsequent decrease in urine osmolality (ability to concentrate urine), is an important cause of nocturnal polyuria. As the mechanism, physicians should pay attention to decreased rates of physiological renal excretion associated with aging and congestive heart disease. The edema ratio calculated from the extracellular fluid volume tends to increase from daytime to bedtime in elderly people with nocturia [15]. These findings suggest that excessive fluid intake may increase the edema ratio at night and decrease the ability to concentrate urine, thereby inducing nocturnal polyuria.

Another possible cause is an age-related change in the diurnal variation of AVP secretion. In response to increased plasma osmolality associated with increased extracellular fluid volume, AVP secretion is usually enhanced and urinary excretion is suppressed. The response is inadequate in some pathological conditions; thirst occurs as a manifestation of fluid homeostasis (host defense response) following nocturnal polyuria, which results in drinking behavior [16]. In elderly people, fluid restrictions should therefore be implemented carefully with close monitoring of fluid balance, or they might increase fluid intake at night and worsen their condition. Because the extracellular fluid volume is likely to increase and dehydration is likely to occur, care should be exercised to avoid excessive fluid restrictions.

III-1)-C. Nocturia induced by excessive fluid intake

Fluid intake is recommended for the prevention of ischemic disorders, such as cerebral infarction, myocardial infarction, and angina pectoris, and it is overrated by some individuals. However, only a few studies rigorously examined the preventive effect of excessive fluid intake on ischemic disorders. There are many conditions that cause a substantial increase the endogenous vasopressin level, such as stroke, quick loss of blood pressure, painful conditions such as myocardial infarction, angina pectoris, nausea, etc. This vasopressin increase results in fluid retention which may be harmful for the patient.

In light of this, the change in blood viscosity was investigated after 1 to 2 hours and 1-week of fluid intake, with no significant change observed [17]. The blood viscosity was maintained at about 6% throughout the day [17], suggesting that excessive fluid intake has a minimum effect on blood viscosity. Excessive fluid intake may increase extracellular fluid volume and exacerbate adverse events such as nocturnal polyuria and cardiac overload.

III-1)-D. Drugs and nocturia

Another possible cause of nocturnal polyuria is the influence of drugs used for the treatment of other diseases. Loop diuretics are often prescribed to reduce cardiac overload and lower blood pressure. If a patient does not take furosemide in the afternoon but takes it in the evening and goes to bed at 23:00, the drug does not produce the antihypertensive effect in the daytime but may cause nocturnal polyuria because its half-life is about 6 hours. However, furosemide at oral doses of 40 mg given 6 to 8 hours before bedtime has been reported to improve nocturnal polyuria and natriuresis [18], suggesting that the drug requires careful consideration of dose and time of administration. Care should be exercised when calcium antagonists are used in patients with nocturia because these drugs increase the glomerular filtration rate and have an inhibitory effect on AVP secretion [19]. This is just a sample of the many drugs that influence voiding patterns. In patients with nocturnal polyuria, it is important to obtain detailed information on the type, dose, and administration of medications prescribed to each patient and measure the residual urine volume.

III-1)-E. Hypertension and nocturia

The association between blood pressure and nocturia has been intensively investigated. Healthy people have the circadian rhythm of catecholamine secretion with higher catecholamine levels during the day and lower levels during sleep at night. However, age-related increases in catecholamine secretion influence overall diurnal variation, and the catecholamine levels at night in elderly people with nocturia tend to be higher than those during the day in healthy young people [20].

Increased catecholamines associated with hypertension decrease renal blood flow [21], which increases the circulating blood volume during the day and decreases diurnal urine production. This leads to an increase in nocturnal urine production together with excessive fluid intake. During sleep, people are in a supine position, and catecholamine levels decrease, which increases renal blood flow. This change together with the diuretic effect of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) results in increased nocturnal urine production and polyuria (Appendix 1) [22].

III-1)-F. Regulation of urine volume by BNP

ANP and BNP, which belong to the natriuretic peptide family, are peptide hormones secreted by the heart. Blood levels of these hormones increase with the severity of heart failure under the New York Heart Association (NYHA) classification

doi:10.3834/uij.1939-4810.2008.11.07
ISSN 1944-5792 (print), ISSN1944-5784 (online)

of cardiac function and are therefore useful in estimating the prognosis in heart failure [23].

BNP is a cardiac hormone that is primarily secreted by the ventricle. BNP levels tend to increase with increasing age, and exceed 50 pg/mL in a substantial number of patients [24]. Our study showed that some elderly patients with overactive bladder had high plasma osmolality and BNP levels despite low urine specific gravity [25]. Elevated BNP levels (50 pg/mL or higher) suggest the possibility of concomitant cardiovascular diseases and require a thorough examination [24]. BNP has physiological effects of diuresis and vasodilation and antagonizes the function of the renin-angiotensin-aldosterone system. However, its diuretic effect is weak, and BNP is primarily used as a marker for heart failure. BNP is often correlated positively with the nocturnal urine volume and nocturnal polyuria index (NPi), suggesting the involvement of BNP in nocturnal polyuria [26].

III-1)-G. BNP-based evaluation of nocturnal polyuria and treatment strategy

The following classification of the type of nocturnal polyuria on the basis of BNP levels and NPi with consideration of cardiac function may help clinical diagnosis and treatment [26].

1. Global polyuria type: BNP ≤ 50 pg/mL, NPi < 35%
2. Intermediate type: BNP < 100 pg/mL, NPi < 45%
3. Decreased daytime urine volume, nighttime predominant polyuria type: BNP ≥ 100 pg/mL, NPi ≥ 45%

Nocturnal polyuria classified as the global polyuria type, which is characterized by low BNP levels and low nocturnal urine volume, is not related to cardiac function but might be associated with excessive fluid intake, diabetes mellitus, caffeine intake, or alcohol intake. Effective therapy may therefore include treatment of underlying diseases, instructions regarding fluid intake, diuretics, and desmopressin (DDAVP). The nighttime dominant polyuria type characterized by BNP levels of 100 pg/mL or more and NPi of 45% or more might be associated with hypertension, arteriosclerosis, or heart failure, so particular care should be used in prescribing DDAVP [27]. BNP is sensitive to the change in cardiac load after treatment with DDAVP or diuretics, and therefore BNP monitoring may prevent adverse reactions and complications. Care should also be used with fluid restrictions and treatment with diuretics, and behavioral therapy (such as exercise instruction, afternoon naps with the legs elevated, and use of elastic stockings) together with cardiovascular treatment may play a central role in the treatment.

III-1)-H. Other causes of nocturnal polyuria

Nocturnal polyuria may result from some other causes. Important causes include age-related decreases in renal concentrating ability, congestive heart failure, diabetes mellitus, diabetes insipidus, electrolyte abnormalities, obstructive sleep apnea [28], and inhibitory effect of cold stimulation on AVP secretion [29]. Increased urine volume at night and during the day is found in patients with nocturnal polyuria resulting from causes other than congestive heart failure. The circadian rhythm of AVP might disappear even in healthy elderly people, and excessive body fluids possibly suppress the secretion of AVP.

III-2) REDUCED NOCTURNAL BLADDER CAPACITY

In healthy people, the voided volume per micturition on waking in the morning is about 1.5 to 2 times that during the day. However, an increase in the voided volume per micturition at night and early in the morning is not evident in patients with nocturia. Reduced nocturnal bladder capacity is a manifestation of nocturia. Hypertension is involved in reduced bladder capacity. Elevated levels of circulating catecholamines may lower the threshold bladder volume at which desire to urinate occurs by acting on the spinal adrenergic α_{1D} receptor in the afferent pathway of the micturition reflex and the bladder α_{1D} receptor [20]. Patients with morning hypertension frequently urinate before and after waking, and their blood pressure is often elevated in the same time frame [30]. Circulating catecholamines might also be responsible for the desire to urinate in a tense situation.

Sleep disorders are also involved in reduced bladder capacity. Secretion of melatonin, a sleep substance, tends to decrease with increasing age. Resultant decreases in slow-wave sleep and rapid eye movement sleep and increases in arousal and early morning awakening are responsible for decreased sleep efficiency. The arousal threshold in response to the desire to urinate is lowered with shallow sleep, which induces arousal and nocturnal micturition [15].

Low serum glycine levels might also be involved in reduced bladder capacity [20]. Glycinergic neurons are representative inhibitory interneurons in the spinal cord and inhibit the afferent pathway of the micturition reflex [31]. Serum glycine levels are decreased in patients with spinal cord injury and benign prostatic hyperplasia, and an irreversible decrease in

http://www.urotodayinternationaljournal.com
doi:10.3834/uij.1939-4810.2008.11.07
ISSN 1944-5792 (print), ISSN1944-5784 (online)

the number or activity of glycinergic neurons might cause reduced bladder capacity and frequent micturitions [20]. Flavoxate hydrochloride has recently been reported to activate spinal glycinergic neurons and may become a treatment option for nocturia [32].

In addition, it should be noted that irreversible organic reduction in bladder capacity might result from a prolonged state of functionally reduced bladder capacity that is associated with reduced bladder capacity, overactive bladder due to encephalomyelopathy, voiding habits, a tumor, or calculi.

III-3) EVALUATION OF PATHOLOGICAL CONDITIONS WITH A VOIDING DIARY

Completion of a voiding diary is essential for a scientific, detailed evaluation of voiding patterns [33]. It is preferable to document the time and amount of voiding, the type and amount of fluid intake, the presence or absence as well as the degree of micturition urgency, and the presence or absence of incontinence. In principle, these variables should be documented for 3 days in men and for 4 days in women, and diary records for 2 consecutive days as well as those on working days and holidays should preferably be considered. Analysis of a voiding diary allows evaluation of pathological conditions of polyuria, nocturnal polyuria, and reduced maximum voided volume, as well as calculation of nocturia index (Ni), nocturnal bladder capacity index (NBCi), and NPi (Appendix 2) [34]. Many cases of nocturia are characterized by a mixed type of nocturnal polyuria and reduced nocturnal bladder capacity [19].

III-3)-A. Voiding diary and sleep diary

The diary used in our hospital is shown in Appendix 3. The diary is remarkable in that patients are instructed to strictly distinguish and document the normal desire to void and a sudden compelling desire to void. The usual strong desire to void during storage phase is a normal response, whereas no sensation of bladder filling or desire to void or a sudden compelling desire to pass urine which is difficult to defer represent a pathological conditions; these should be clearly distinguished. The data entry field for first micturition in the morning is allocated on the bottom of the diary, which dramatically reduces missing data and ensures completeness of the diary. Physicians should prepare an example of a completed diary, repeatedly provide patients with instructions on how to complete the diary, instruct patients to record accurate data after each voiding, and reexamine the reliability of the entries by medical interview.

Before starting treatment, we instruct all patients to complete the voiding diary, the International Prostate Symptom Score, King's Health Questionnaire, Pittsburgh Sleep Quality Index, and sleep diary (Appendix 4). A sleep diary allows characterization of sleep patterns and evaluation of pathological conditions including disorders of initiating sleep, reinitiating sleep, and early morning awakening, which are difficult to identify from the number of micturitions alone.

III-3)-B. Evaluation of nocturia with a voiding diary

Classification of nocturia with a voiding diary and causative conditions are shown below:

1. Polyuria type: Excessive fluid intake, drugs, diabetes mellitus, diabetes insipidus, congestive heart failure, AVP secretion abnormalities, and others
2. Reduced maximum voided volume (MVV) type: Overactive bladder, habit, psychogenic, interstitial cystitis, carcinoma in situ, sleep disorder, and others
3. Mixed type of the two

III-4) GLOBAL POLYURIA

Global polyuria is also a cause of nocturia. The diagnostic criterion for all-day polyuria is a 24-hour urine volume of 40 mL/kg or more. It is characterized by overproduction of urine during the day and night and may be caused by diabetes mellitus, diabetes insipidus, and polydipsia.

Diabetes mellitus is a typical disease accompanying increased urine volume, and treatment of diabetes mellitus improves polyuria. Diabetes insipidus is classified into central and nephrogenic diseases according to the presence or absence of urine concentration during a water deprivation test and response to AVP. Central diabetes insipidus may be treated with AVP administration [35], whereas nephrogenic diabetes insipidus is primarily managed by instructions regarding fluid intake because this condition is caused by impaired response to AVP in the kidney.

Patients with polydipsia have a normal ability to concentrate urine as revealed by a water deprivation test but complain of severe thirst. Polydipsia is most likely due to central causes in patients with previous head injury or radiotherapy and psychogenic causes in patients without. Psychogenic polydipsia is more common. It is important to provide consultation and instructions regarding lifestyle modification and fluid intake to patients with psychogenic polydipsia.

http://www.urotodayinternationaljournal.com
doi:10.3834/uij.1939-4810.2008.11.07
ISSN 1944-5792 (print), ISSN1944-5784 (online)

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III-5) SLEEP DISORDERS

III-5)-A. Sleep disorders and mental and physical health

A sleep disorder is a pathological condition closely associated with nocturia. Sleep is closely associated with mental and physical health, and a sleep disorder often causes health problems. An epidemiological study reported that less than 6.5 hours of sleep or 8 or more hours of sleep increased the risk of health problems [36], and another report indicated that 50% of patients with insomnia received treatment for conditions other than a sleep disorder within 12 months. A sleep disorder has a wide range of effects on health, including a decrease in immune function [37], increase in the incidence of ischemic heart disease and cerebrovascular dementia [38], decrease in cognitive function, risk factor for Alzheimer's disease, and impaired memory and concentration, leading to impairment of physical and mental quality of life [39].

Sleep disorder-induced memory impairment may be explained by sleep interruptions and a resultant decrease in rapid eye movement sleep. Rapid eye movement sleep is believed to be involved in the process of memory consolidation [40], and its decrease may reduce learning ability, social cooperativeness, and satisfaction with life [41]. The use of hypnotics for the treatment of sleep disorders should be avoided as much as possible because it is associated with risks of memory and cognitive disorders. Priority should be given to modification of sleep habits and lifestyle as well as improvement of sleep hygiene using behavioral therapy, and drug therapy should be started with a (ultra) short-acting agent only if clearly needed.

III-5)-B. Sleep disorders due to arousal in elderly people

Elderly people experience behavioral arousal, light arousal, and exposure to cold stimulation when voiding at night, which activate the sympathetic nervous system and make it difficult to fall sleep again. Quality of sleep is significantly influenced by the number of nocturnal micturitions as well as the presence or absence of micturition at the time of arousal and early morning awakening; whether or not the person smoothly reinitiates sleep is also a very significant factor [42]. Cold may act diuretic by depression of the circulating vasopressin level. Low temperature in the bedroom might therefore be harmful for certain elderly persons [43].

Tanaka *et al.* [44] reported that patients with insomnia for a duration of one month accounted for 7.1% of people in their 60s, 9.9% of people in their 70s, and 17.6% of people in their 80s and that the disorder of maintaining sleep due to arousal was more common than difficulty falling asleep. Among all factors, nocturia was found to contribute most significantly to a disorder of maintaining sleep with a contribution rate of 0.447 [45], and there was a close association between the number of nocturnal micturitions and the frequency of arousal. Compared with persons without long-term insomnia, patients with long-term insomnia had significantly more frequent nocturnal micturitions (3 or more times, 23.8%; 2 or more times, 55.6%) [44]. In elderly people, long-term insomnia is inextricably linked to nocturia. Nocturia and sleep interact in a negative way. Poor sleep increases nocturia and nocturia deteriorates sleep.

III-5)-C. Influence of sleep disorders on nocturia

The relationship between sleep disorders and nocturia might be summarized as follows [46]:

1. Impairment of quality of sleep with increasing age and nocturia associated with frequent arousal and disorder of reinitiating sleep
2. Disorder of maintaining sleep associated with nocturia caused by BPH and other urologic diseases
3. Nocturia (2% of elderly people, about 20% to 30% of patients with dialysis) associated with specific symptoms, such as restless legs syndrome [47]
4. Nocturia resulting from a lack of diurnal variation of AVP associated with circadian rhythm abnormalities (the lack of nocturnal AVP rise)

In most cases, there is no substantial difference in daily urine volume [48]. The understanding of voiding patterns, fluid intake, and sleep conditions combined with the use of a voiding diary is essential in developing a treatment strategy.

III-6) SUMMARY OF PATHOLOGICAL CONDITIONS

To understand the pathological conditions of nocturia, it is important to examine the overall daily lifestyle and take into consideration aging, cardiac function (blood pressure), glucose tolerance, respiratory function, endocrine environment (AVP and catecholamines), and diurnal variation (Appendix 5).

CONCLUSION

Approaches to nocturia, a condition induced by a variety of causes, require minimally invasive, low-cost, reasonable, and accurate identification of the pathological conditions. To improve the physical and mental quality of life as well as activities of daily living, physicians should constantly monitor the pathological conditions and take flexible, proactive approaches.

http://www.urotodayinternationaljournal.com
doi:10.3834/uij.1939-4810.2008.11.07
ISSN 1944-5792 (print), ISSN1944-5784 (online)

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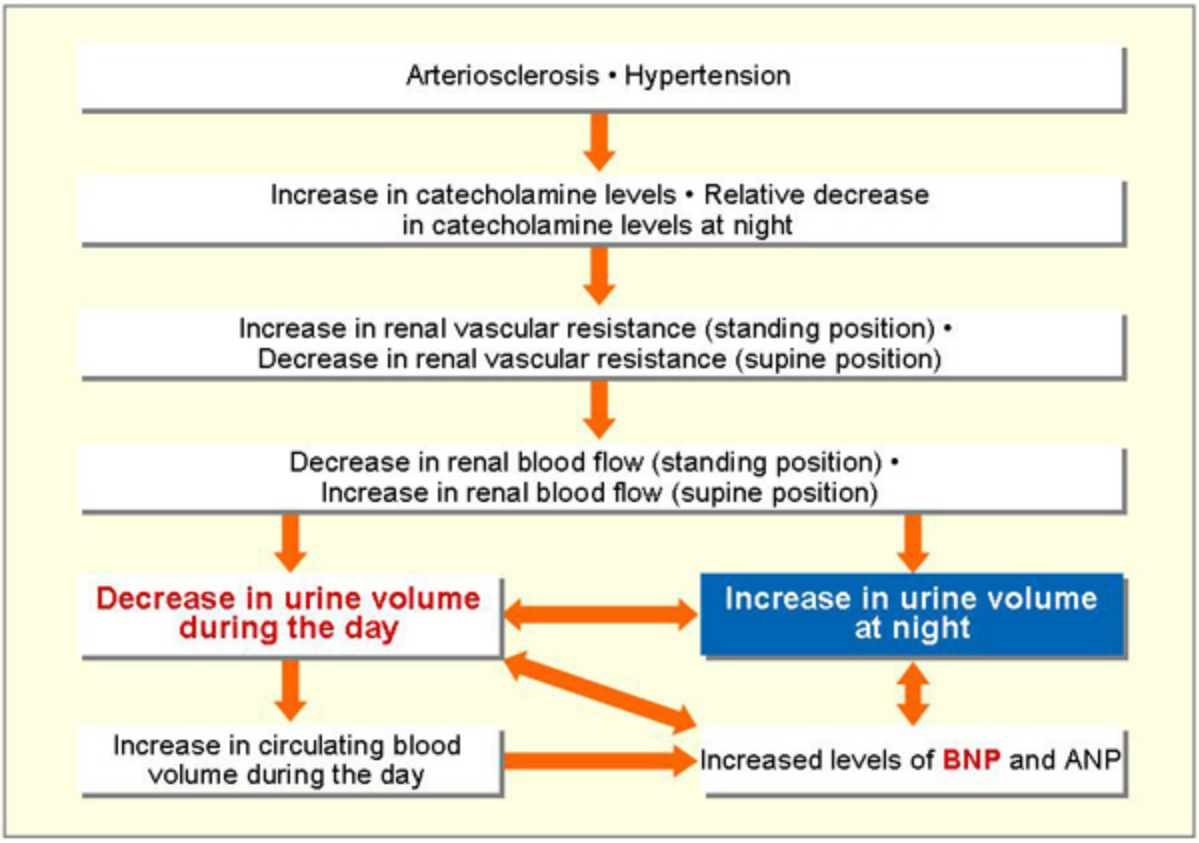
TO CITE THIS ARTICLE: Oh-oka H, Sone A, Sugaya K, Nishizawa O. Pathogenesis and Diagnosis of Nocturia: From a New Viewpoint. UIJ. 2008 Dec;1(5). doi:10.3834/uij.1939-4810.2008.11.07

Appendix 1. Hypertension and nocturnal polyuria

doi: 10.3834/uij.1939.4810.2008.11.07.a1



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Appendix 2. Evaluation on the basis of voiding diary

doi: 10.3834/uij.1939.4810.2008.11.07.a2

◆ **Conditions evaluated with a voiding diary**

- Polyuria: Daily urine volume ≥ 40 mL/kg
- Nocturnal polyuria: Nocturnal urine volume ≥ 10 mL/kg or the ratio of nocturnal urine volume to daily urine volume ≥ 33% to 35%
- Functionally reduced bladder capacity: Maximum voided volume per micturition ≤ 4 mL/kg

◆ **Parameters calculated from voiding diary data**

- Nocturia index (Ni; Nocturnal urine volume ÷ Functional bladder capacity [or Maximum voided volume per micturition]): Ni > 1 → nocturia
- Nocturnal bladder capacity index (NBCi)=Actual number of nightly voids (ANV)-Predicted number of nightly voids (PNV=Ni-1)
  NBCi > 0 → Reduced nocturnal bladder capacity
- Nocturnal polyuria index (NPi; Nocturnal urine volume ÷ 24-hour urine volume): NPi > 33% → nocturnal polyuria

doi:10.3834/uij.1939-4810.2008.11.07
http://www.urotodayinternationaljournal.com
ISSN 1944-5792 (print), ISSN1944-5784 (online)

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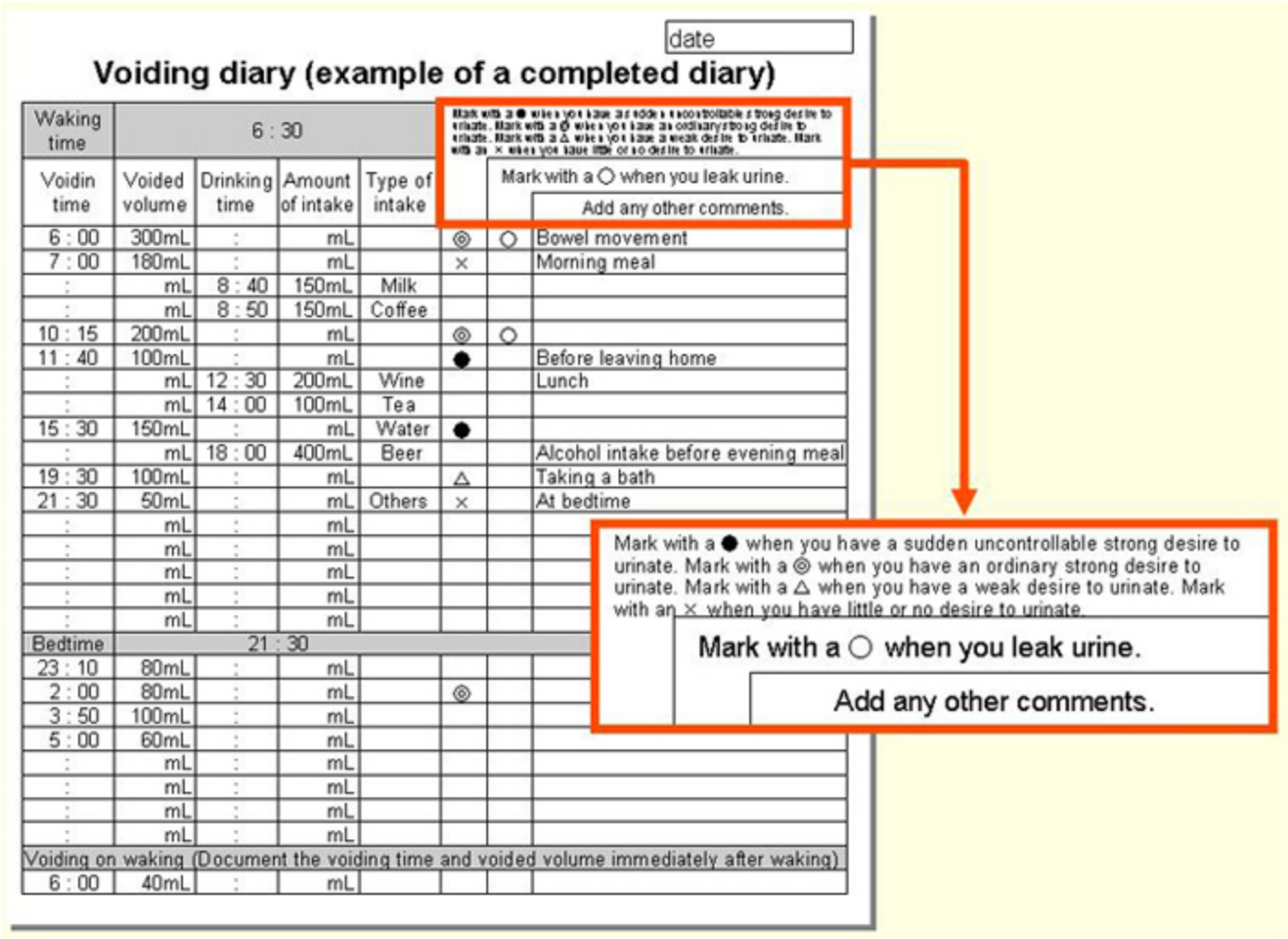
Appendix 3. Original voiding diary (example)

doi: 10.3834/uij.1939.4810.2008.11.07.a3



date

Voiding diary (example of a completed diary)

Waking time	6 : 30						
Voidin time	Voided volume	Drinking time	Amount of intake	Type of intake			
6 : 00	300mL	:	mL		◎	○	Bowel movement
7 : 00	180mL	:	mL		×		Morning meal
:	mL	8 : 40	150mL	Milk			
:	mL	8 : 50	150mL	Coffee			
10 : 15	200mL	:	mL		◎	○	
11 : 40	100mL	:	mL		●		Before leaving home
:	mL	12 : 30	200mL	Wine			Lunch
:	mL	14 : 00	100mL	Tea			
15 : 30	150mL	:	mL	Water	●		
:	mL	18 : 00	400mL	Beer			Alcohol intake before evening meal
19 : 30	100mL	:	mL		△		Taking a bath
21 : 30	50mL	:	mL	Others	×		At bedtime
:	mL	:	mL				
:	mL	:	mL				
:	mL	:	mL				
:	mL	:	mL				
:	mL	:	mL				
Bedtime	21 : 30						
23 : 10	80mL	:	mL				
2 : 00	80mL	:	mL		◎		
3 : 50	100mL	:	mL				
5 : 00	60mL	:	mL				
:	mL	:	mL				
:	mL	:	mL				
:	mL	:	mL				
:	mL	:	mL				
Voiding on waking (Document the voiding time and voided volume immediately after waking)							
6 : 00	40mL	:	mL				

Mark with a ● when you have a sudden uncontrollable strong desire to urinate. Mark with a ◎ when you have an ordinary strong desire to urinate. Mark with a △ when you have a weak desire to urinate. Mark with an × when you have little or no desire to urinate.

Mark with a ○ when you leak urine.

Add any other comments.

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Appendix 4. Sleep diary (with an example of a completed diary)

doi: 10.3834/uij.1939.4810.2008.11.07.a4

Sleep diary (for 1 week)

	Time (0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24)	Time to sleep (min)	Sleeping hours (hr min)
Mon			
Tue			
Wed			
Thu			
Fri			
Sat			
Sun			

How to fill in the sleep diary (Recall your sleep and sleepiness in the previous 24 hours)

- ■ Fill in your sleeping hours with black.
- ▨ Fill in your waking hours in bed with oblique lines.
- ⟷ Mark your sleepy hours with arrows.
- × Mark your medication time with X.

Record the time elapsed from lights off to sleep onset.

Record your net sleeping hours excluding waking hours in bed.

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Appendix 5. Summary of pathological conditions

doi: 10.3834/uij.1939.4810.2008.11.07.a5